WEST Search History

DATE: Thursday, July 17, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB; PLUR=YES; OP=ADJ			
L13	(5851812)![pn]	1	L13
L12	ikappa-b-related or i-kappa-b-related	1	L12
L11	Likappa-b-related or i-kappa-b-related	1	L11
L10	ikappab-r	0	L10
L9	L8 and l2	55	L9
L8	ikappab	81	L8
L7	l5 not l1	1	L7
L6	inhibitor-kappab-r	0	L6
L5	inhibitor-kappa b-r	2	L5
L4	inhibitor-kappa b-rL3	0	L4
L3	L2 and l1	1	L3
L2	antisense or anti-sense	32368	L2
L1	nfkbil2	2	L1

END OF SEARCH HISTORY

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PASSWORD:
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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:34:08 ON 17 JUL 2003

=> file medline biotechno caplus scisearch biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'BIOTECHNO' ENTERED AT 10:34:49 ON 17 JUL 2003
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FILE 'BIOSIS' ENTERED AT 10:34:49 ON 17 JUL 2003
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=> s antisense or antisense
L1      105655 ANTISENSE OR ANTISENSE

=> s antisense or anti-sense
L2      108810 ANTISENSE OR ANTI-SENSE

=> s nfkbil2
L3            4 NFKBIL2

=> s l3 and l2
L4            0 L3 AND L2

=> s ribozyme or ribozymes
L5        20278 RIBOZYME OR RIBOZYMES

=> s l5 and l3
L6            0 L5 AND L3

=> s inhibitor-kappa b-r
L7            1 INHIBITOR-KAPPA B-R

=> s l7 and l2
L8            1 L7 AND L2

=> d ab

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AB   Antisense compds., compns. and methods are provided for
     modulating the expression of inhibitor-kapp B-R.  The compns. comprise
     antisense compds., particularly antisense
     oligonucleotides, targeted to nucleic acids encoding inhibitor-
     kappa B-R.  Methods of using these compds. for
     modulation of inhibitor-kappa B-R
     expression and for treatment of diseases assocd. with expression of
     inhibitor-kappa B-R are provided.


=> d
```

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2003:396997 CAPLUS
DN 138:396185
TI **Antisense** modulation of inhibitor-kappa B-related expression for treatment of microbial infections
IN Monia, Brett P.; Watt, Andrew T.
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003042360	A2	20030522	WO 2002-US35597	20021105
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003105040	A1	20030605	US 2001-993731	20011113
PRAI	US 2001-993731	A	20011113		

```
=> s nfkbil2)
UNMATCHED RIGHT PARENTHESIS 'NFKBIL2)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ikappab
L9        4266 IKAPPAB

=> s l9 and l2
L10        106 L9 AND L2

=> l10 and ikappab-r
L10 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l10 and ikappab-r
L11          0 L10 AND IKAPPAB-R

=> s ikappab-r
L12          0 IKAPPAB-R

=> dup rem l10
PROCESSING COMPLETED FOR L10
L13          63 DUP REM L10 (43 DUPLICATES REMOVED)

=> d ti-63
'TI-63' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end
```

=> d ti 1-63

L13 ANSWER 1 OF 63 MEDLINE DUPLICATE 1
TI Inhibition of tumor necrosis factor alpha-mediated NFkappaB activation and leukocyte adhesion, with enhanced endothelial apoptosis, by G protein-linked receptor (TP) ligands.

L13 ANSWER 2 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 2
TI A central role for the JNK pathway in mediating the antagonistic activity of pro-inflammatory cytokines against transforming growth factor-beta-driven SMAD3/4-specific gene expression

L13 ANSWER 3 OF 63 MEDLINE DUPLICATE 3
TI Resistance of human ovarian cancer cells to tumor necrosis factor alpha is a consequence of nuclear factor kappaB-mediated induction of Fas-associated death domain-like interleukin-1beta-converting enzyme-like inhibitory protein.

L13 ANSWER 4 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI Neuroprotective effects of IGF-I against TNF alpha-induced neuronal damage in HIV-associated dementia

L13 ANSWER 5 OF 63 MEDLINE DUPLICATE 4
TI Antiapoptotic effect of interferon-alpha on hepatic stellate cells (HSC): a novel pathway of IFN-alpha signal transduction via Janus kinase 2 (JAK2) and caspase-8.

L13 ANSWER 6 OF 63 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
TI Modulation of gene expression associated with inflammation, proliferation and neurite outgrowth using antisense and enzymic nucleic acid-based technologies

L13 ANSWER 7 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Protein and cDNA sequences of a 37.40-kilodalton human I.kappa.B protein kinase-like protein and their therapeutic uses

L13 ANSWER 8 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Protein and cDNA sequences of human **IkappaB** kinase 15 and therapeutical uses

L13 ANSWER 9 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 6
TI Aldose reductase mediates mitogenic signaling in vascular smooth muscle cells

L13 ANSWER 10 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI NADPH oxidase promotes NF-.kappa.B activation and proliferation in human airway smooth muscle

L13 ANSWER 11 OF 63 MEDLINE DUPLICATE 7
TI Nuclear factor kappaB-mediated induction of Flice-like inhibitory protein prevents tumor necrosis factor alpha-induced apoptosis in rat granulosa cells.

L13 ANSWER 12 OF 63 MEDLINE DUPLICATE 8
TI Inhibition of cell proliferation and AP-1 activity by acrolein in human A549 lung adenocarcinoma cells due to thiol imbalance and covalent modifications.

L13 ANSWER 13 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI 1 alpha,25-dihydroxyvitamin D-3 stimulates phosphorylation of I kappa B alpha and synergizes with TPA to induce nuclear translocation of NF kappa B during monocytic differentiation of NB4 leukemia cells

L13 ANSWER 14 OF 63 MEDLINE
TI Selective binding of nucleotide probes by eosinophilic cationic protein during in situ hybridisation.

L13 ANSWER 15 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISIDUPLICATE 9
TI Stable inhibition of NF-kappa B in salivary gland cells does not enhance sensitivity to TNF-alpha-induced apoptosis due to upregulation of TRAF-1 expression

L13 ANSWER 16 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI Heat shock inhibits TNF-induced ICAM-1 expression in human endothelial cells via I kappa kinase inhibition

L13 ANSWER 17 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Tumor Necrosis Factor-Alpha Effects on Rat Gastric Enterochromaffin-Like Cells

L13 ANSWER 18 OF 63 MEDLINE DUPLICATE 10
TI Nuclear factor-kappa B activation pathway in intestinal epithelial cells is a major regulator of chemokine gene expression and neutrophil migration induced by Bacteroides fragilis enterotoxin.

L13 ANSWER 19 OF 63 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI CRITICAL ROLE OF GADD153 IN MUTANT PRESENILIN SENSITIVITY TO STRESS - INDUCED DEATH.

L13 ANSWER 20 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Kinase suppressor of Ras determines survival of intestinal epithelial cells exposed to tumor necrosis factor

L13 ANSWER 21 OF 63 MEDLINE DUPLICATE 11
TI SIMPL is a tumor necrosis factor-specific regulator of nuclear factor-kappaB activity.

L13 ANSWER 22 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI The atypical protein kinase C-interacting protein p62 is a scaffold for NF-.kappa.B activation by nerve growth factor

L13 ANSWER 23 OF 63 MEDLINE
TI The Src-protein tyrosine kinase Lck is required for IL-1-mediated costimulatory signaling in Th2 cells.

L13 ANSWER 24 OF 63 MEDLINE
TI RNA-dependent protein kinase PKR is required for activation of NF-kappa B by IFN-gamma in a STAT1-independent pathway.

L13 ANSWER 25 OF 63 MEDLINE
TI NF-kappaB/RelA transactivation is required for atypical protein kinase C iota-mediated cell survival.

L13 ANSWER 26 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Constitutive activation of nuclear factor-.kappa.B prevents TRAIL-induced apoptosis in renal cancer cells

L13 ANSWER 27 OF 63 MEDLINE
TI The inhibitory action of sodium arsenite on lipopolysaccharide-induced nitric oxide production in RAW 267.4 macrophage cells: a role of Raf-1 in lipopolysaccharide signaling.

L13 ANSWER 28 OF 63 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Nonactivated microglia promote oligodendrocyte precursor survival and maturation through the transcription factor NF-kappaB.

L13 ANSWER 29 OF 63 MEDLINE DUPLICATE 12

TI Oncostatin M promotes biphasic tissue factor expression in smooth muscle cells: evidence for Erk-1/2 activation.

L13 ANSWER 30 OF 63 MEDLINE DUPLICATE 13
TI Role of increased basal expression of heat shock protein 72 in colonic epithelial c2BBE adenocarcinoma cells.

L13 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Human E3 ubiquitin ligase and .beta.TrCP and methods for modulating ubiquitination of phospho-I.kappa.B and activation of NF-.kappa.b and disease treatment

L13 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI **Antisense** oligonucleotides for inhibiting Inhibitor-.kappa.B kinase subunit expression

L13 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 14
TI The I.kappa.B kinase (IKK) complex is tripartite and contains IKK.gamma. but not IKAP as a regular component

L13 ANSWER 34 OF 63 MEDLINE DUPLICATE 15
TI NF-kappaB inhibits apoptosis in murine mammary epithelia.

L13 ANSWER 35 OF 63 MEDLINE DUPLICATE 16
TI Nuclear factor-kappaB/**IkappaB** signaling pathway may contribute to the mediation of paclitaxel-induced apoptosis in solid tumor cells.

L13 ANSWER 36 OF 63 MEDLINE DUPLICATE 17
TI Protein kinase C-theta participates in NF-kappaB activation induced by CD3-CD28 costimulation through selective activation of **IkappaB** kinase beta.

L13 ANSWER 37 OF 63 MEDLINE DUPLICATE 18
TI Activation of the heterodimeric **IkappaB** kinase alpha (IKKalpha)-IKKbeta complex is directional: IKKalpha regulates IKKbeta under both basal and stimulated conditions.

L13 ANSWER 38 OF 63 MEDLINE DUPLICATE 19
TI Gene therapy that inhibits nuclear translocation of nuclear factor kappaB results in tumor necrosis factor alpha-induced apoptosis of human synovial fibroblasts.

L13 ANSWER 39 OF 63 MEDLINE DUPLICATE 20
TI Dehydration activates an NF-kappaB-driven, COX2-dependent survival mechanism in renal medullary interstitial cells.

L13 ANSWER 40 OF 63 MEDLINE DUPLICATE 21
TI Inhibition with **antisense** oligonucleotide suggests that **IkappaB**-alpha does not form a negative autoregulatory loop for NF-kappaB in mesangial cells.

L13 ANSWER 41 OF 63 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Oncostatin M promotes prolonged tissue factor expression in smooth muscle cells: Evidence for ERK-1/2 activation of NF-kappaB.

L13 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI Human I.kappa.B kinase .beta. subunit (IKK.beta.), its cDNA sequences, recombinant expression, and use in treating inflammation and in identifying anti-inflammatory drugs

L13 ANSWER 43 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI **Antisense** modulation of Inhibitor-.kappa.B kinase-.alpha. expression

L13 ANSWER 44 OF 63 MEDLINE DUPLICATE 22
TI Insulin antiapoptotic signaling involves insulin activation of the nuclear factor kappaB-dependent survival genes encoding tumor necrosis factor receptor-associated factor 2 and manganese-superoxide dismutase.

L13 ANSWER 45 OF 63 MEDLINE DUPLICATE 23
TI Tumor necrosis factor induces Bcl-2 and Bcl-x expression through NFkappaB activation in primary hippocampal neurons.

L13 ANSWER 46 OF 63 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 24
TI Regulation of NF-.kappa.B activity by I.kappa.B-related proteins in adenocarcinoma cells

L13 ANSWER 47 OF 63 MEDLINE DUPLICATE 25
TI Induction of monocyte chemoattractant protein-1 by albumin is mediated by nuclear factor kappaB in proximal tubule cells.

L13 ANSWER 48 OF 63 MEDLINE DUPLICATE 26
TI Interleukin-1-induced nuclear factor-kappaB-IkappaBalpha autoregulatory feedback loop in hepatocytes. A role for protein kinase calpha in post-transcriptional regulation of ikappabalpha resynthesis.

L13 ANSWER 49 OF 63 MEDLINE DUPLICATE 27
TI Extracellular matrix inhibits apoptosis and enhances endothelial cell differentiation by a NfkappaB-dependent mechanism.

L13 ANSWER 50 OF 63 MEDLINE DUPLICATE 28
TI Nuclear factor kappaB cooperates with c-Myc in promoting murine hepatocyte survival in a manner independent of p53 tumor suppressor function.

L13 ANSWER 51 OF 63 MEDLINE DUPLICATE 29
TI TGF-beta1 inhibits NF-kappaB activity through induction of **IkappaB** -alpha expression in human salivary gland cells: a possible mechanism of growth suppression by TGF-beta1.

L13 ANSWER 52 OF 63 MEDLINE DUPLICATE 30
TI Rel transcription factors contribute to elevated urokinase expression in human ovarian carcinoma cells.

L13 ANSWER 53 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI I.kappa.b kinase, its subunits and sequences, and methods for their use

L13 ANSWER 54 OF 63 MEDLINE DUPLICATE 31
TI Fluid shear stress activation of **IkappaB** kinase is integrin-dependent.

L13 ANSWER 55 OF 63 MEDLINE
TI Implication of a multisubunit Ets-related transcription factor in synaptic expression of the nicotinic acetylcholine receptor.

L13 ANSWER 56 OF 63 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI NFkappaB and inflammatory bowel disease.

L13 ANSWER 57 OF 63 MEDLINE DUPLICATE 32
TI Activation of NF-kappaB mediates the PMA-induced differentiation of K562 cells.

L13 ANSWER 58 OF 63 MEDLINE
TI The NF-kappaB/Rel family of proteins mediates Abeta-induced neurotoxicity and glial activation.

L13 ANSWER 59 OF 63 MEDLINE
TI The immediate-early gene product MAD-3/EDG-3/**IkappaB** alpha is an endogenous modulator of fibroblast growth factor-1 (FGF-1) dependent human

endothelial cell growth.

L13 ANSWER 60 OF 63 MEDLINE
TI Activation of the retinoblastoma gene expression by Bcl-3: implication for muscle cell differentiation.

L13 ANSWER 61 OF 63 CAPLUS COPYRIGHT 2003 ACS
TI The role of the dsRNA-activated kinase, PKR, in signal transduction

L13 ANSWER 62 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI EVIDENCE FOR DIFFERENTIAL FUNCTIONS OF THE P50 AND P65 SUBUNITS OF NF-KAPPA-B WITH A CELL-ADHESION MODEL

L13 ANSWER 63 OF 63 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI CACTUS, A GENE INVOLVED IN DORSOVENTRAL PATTERN-FORMATION OF DROSOPHILA, IS RELATED TO THE I-KAPPA-B GENE FAMILY OF VERTEBRATES

=> d 32 35 36 40 37 ab

L13 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2003 ACS
AB **Antisense** oligonucleotides having complementary sequences to I-.kappa.B kinase subunit, (IKK-.alpha., IKK-.beta., IKK-.gamma., and CHUK (conserved helix-loop-helix ubiquitous kinase)) gene sequences are provided for inhibiting the expression of cytokines. Interleukin-6 expression, specifically, is inhibited. Phosphorothioate **antisense** oligonucleotides were synthesized. Inhibition of IL-6 expression by those **antisense** oligonucleotides was confirmed in human cell lines.

L13 ANSWER 35 OF 63 MEDLINE DUPLICATE 16
AB Paclitaxel (Taxol), a naturally occurring antimitotic agent, has shown significant cell-killing activity in a variety of tumor cells through induction of apoptosis. The mechanism by which paclitaxel induces cell death is not entirely clear. Recent studies in our laboratory demonstrated that glucocorticoids selectively inhibited paclitaxel-induced apoptosis without affecting the ability of paclitaxel to induce microtubule bundling and mitotic arrest. This finding suggests that apoptotic cell death induced by paclitaxel may occur via a pathway independent of mitotic arrest. In the current study, through analyses of a number of apoptosis-associated genes or regulatory proteins, we discovered that paclitaxel significantly down-regulated **IkappaB** -alpha, the cytoplasmic inhibitor of transcription factor nuclear factor-kappaB (NF-kappaB), which in turn promoted the nuclear translocation of NF-kappaB and its DNA binding activity. In contrast, we found that glucocorticoids could antagonize paclitaxel-mediated NF-kappaB nuclear translocation and activation through induction of **IkappaB** -alpha protein synthesis. Northern blotting analyses demonstrated that the steady-state level of **IkappaB**-alpha mRNA was not affected by paclitaxel, which suggests that the down-regulation of **IkappaB** -alpha by paclitaxel is attributable to protein degradation rather than suppression of transcription. Furthermore, through transfection assays, we demonstrated that tumor cells stably transfected with **antisense** **IkappaB**-alpha expression vectors remarkably increased their sensitivity to paclitaxel-induced apoptosis. Finally, we found that a key subunit of **IkappaB** kinase (IKK) complex, IKKbeta, was up-regulated by paclitaxel, which implies that paclitaxel might down-regulate **IkappaB**-alpha through modulation of IKKbeta activity. All of these results suggest that the NF-kappaB/**IkappaB** -alpha signaling pathway may contribute to the mediation of paclitaxel-induced cell death in solid tumor cells.

L13 ANSWER 36 OF 63 MEDLINE DUPLICATE 17
AB The NF-kappaB/Rel family of eukaryotic transcription factors plays an

essential role in the regulation of inflammatory, antiapoptotic, and immune responses. NF-kappaB is activated by many stimuli including costimulation of T cells with ligands specific for the T-cell receptor (TCR)-CD3 complex and CD28 receptors. However, the signaling intermediates that transduce these costimulatory signals from the TCR-CD3 and CD28 surface receptors leading to nuclear NF-kappaB expression are not well defined. We now show that protein kinase C-theta (PKC-theta), a novel PKC isoform, plays a central role in a signaling pathway induced by CD3-CD28 costimulation leading to activation of NF-kappaB in Jurkat T cells. We find that expression of a constitutively active mutant of PKC-theta potently induces NF-kappaB activation and stimulates the RE/AP composite enhancer from the interleukin-2 gene. Conversely, expression of a kinase-deficient mutant or **antisense** PKC-theta selectively inhibits CD3-CD28 costimulation, but not tumor necrosis factor alpha-induced activation of NF-kappaB in Jurkat T cells. The induction of NF-kappaB by PKC-theta is mediated through the activation of **IkappaB** kinase beta (IKKbeta) in the absence of detectable IKKalpha stimulation. PKC-theta acts directly or indirectly to stimulate phosphorylation of IKKbeta, leading to activation of this enzyme. Together, these results implicate PKC-theta in one pathway of CD3-CD28 costimulation leading to NF-kappaB activation that is apparently distinct from that involving Cot and NF-kappaB-inducing kinase (NIK). PKC-theta activation of NF-kappaB is mediated through the selective induction of IKKbeta, while the Cot- and NIK-dependent pathway involves induction of both IKKalpha and IKKbeta.

L13 ANSWER 40 OF 63 MEDLINE DUPLICATE 21
AB The **IkappaB** proteins are important in the regulation of the NF-kappaB/Rel group of transcription factors which are pivotal in the inflammatory response. **IkappaB**-alpha is itself upregulated by activation of NF-kappaB and is postulated to be part of a negative feedback loop. This role of **IkappaB**-alpha has been challenged, however, by recent evidence that demonstrates (1) continued activation of NF-kappaB in mesangial and endothelial cells despite the resynthesis of **IkappaB**-alpha protein and (2) that inhibition of the transactivating activity of NF-kappaB by corticosteroids can be dissociated from a rise in **IkappaB**-alpha protein. We investigated the role of **IkappaB**-alpha in mesangial cells using a phosphorothioate **antisense** oligonucleotide directed against the translational start point of **IkappaB**-alpha. If **IkappaB**-alpha does function as a negative feedback inhibitor in these cells, then reducing **IkappaB**-alpha levels should lead to an increase in NF-kappaB activity. We first demonstrated that **IkappaB**-alpha protein resynthesis following stimulation could be specifically reduced. We then showed that NF-kappaB DNA binding was not increased with **antisense** treatment following stimulation. Finally, NF- kappaB-dependent gene signalling after stimulation (determined through an NF-kappaB luciferase reporter and upregulation of the mRNA of known NF-kappaB-responsive genes MCP-1 and **IkappaB** -alpha) was reduced rather than increased. These data suggest that **IkappaB**-alpha does not form a negative autoregulatory loop for NF-kappaB in mesangial cells and may actually reduce NF-kappaB activity. This may have relevance to therapies directed at inhibition of NF-kappaB activity in mesangial cell diseases.

L13 ANSWER 37 OF 63 MEDLINE DUPLICATE 18
AB Signal-induced nuclear expression of the eukaryotic NF-kappaB transcription factor involves the stimulatory action of select mitogen-activated protein kinase kinase kinases on the **IkappaB** kinases (IKKalpha and IKKbeta) which reside in a macromolecular signaling complex termed the signalsome. While genetic studies indicate that IKKbeta is the principal kinase involved in proinflammatory cytokine-induced **IkappaB** phosphorylation, the function of the

equivalently expressed IKKalpha is less clear. Here we demonstrate that assembly of IKKalpha with IKKbeta in the heterodimeric signalsome serves two important functions: (i) in unstimulated cells, IKKalpha inhibits the constitutive **IkappaB** kinase activity of IKKbeta; (ii) in activated cells, IKKalpha kinase activity is required for the induction of IKKbeta. The introduction of kinase-inactive IKKalpha, activation loop mutants of IKKalpha, or IKKalpha **antisense** RNA into 293 or HeLa cells blocks NIK (NF-kappaB-inducing kinase)-induced phosphorylation of the IKKbeta activation loop occurring in functional signalsomes. In contrast, catalytically inactive mutants of IKKbeta do not block NIK-mediated phosphorylation of IKKalpha in these macromolecular signaling complexes. This requirement for kinase-proficient IKKalpha to activate IKKbeta in heterodimeric IKK signalsomes is also observed with other NF-kappaB inducers, including tumor necrosis factor alpha, human T-cell leukemia virus type 1 Tax, Cot, and MEKK1. Conversely, the theta isoform of protein kinase C, which also induces NF-kappaB/Rel, directly targets IKKbeta for phosphorylation and activation, possibly acting through homodimeric IKKbeta complexes. Together, our findings indicate that activation of the heterodimeric IKK complex by a variety of different inducers proceeds in a directional manner and is dependent on the kinase activity of IKKalpha to activate IKKbeta.

=> d 32 35 36 37 40

L13 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2003 ACS
AN 2000:657761 CAPLUS
DN 133:248675
TI **Antisense** oligonucleotides for inhibiting Inhibitor-.kappa.B kinase subunit expression
IN Kamiya, Kinya
PA Toa Gosei Chemical Industry Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2000253884	A2	20000919	JP 1999-63291	19990310
PRAI	JP 1999-63291		19990310		

L13 ANSWER 35 OF 63 MEDLINE DUPLICATE 16
AN 2000426001 MEDLINE
DN 20424189 PubMed ID: 10969788
TI Nuclear factor-kappaB/**IkappaB** signaling pathway may contribute to the mediation of paclitaxel-induced apoptosis in solid tumor cells.
AU Huang Y; Johnson K R; Norris J S; Fan W
CS Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston 29425, USA.
NC CA 71851 (NCI)
CA 82440 (NCI)
SO CANCER RESEARCH, (2000 Aug 15) 60 (16) 4426-32.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000922
Last Updated on STN: 20020919
Entered Medline: 20000914

L13 ANSWER 36 OF 63 MEDLINE DUPLICATE 17

AN 2000198478 MEDLINE
DN 20198478 PubMed ID: 10733597
TI Protein kinase C-theta participates in NF-kappaB activation induced by CD3-CD28 costimulation through selective activation of **IkappaB** kinase beta.
AU Lin X; O'Mahony A; Mu Y; Geleziunas R; Greene W C
CS Gladstone Institute of Virology and Immunology, Departments of Medicine and Microbiology and Immunology, University of California, San Francisco, California 94141, USA.
NC MH 59037 (NIMH)
SO MOLECULAR AND CELLULAR BIOLOGY, (2000 Apr) 20 (8) 2933-40.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000505
Last Updated on STN: 20020420
Entered Medline: 20000425

L13 ANSWER 37 OF 63 MEDLINE DUPLICATE 18
AN 2000115862 MEDLINE
DN 20115862 PubMed ID: 10648602
TI Activation of the heterodimeric **IkappaB** kinase alpha (IKKalpha)-IKKbeta complex is directional: IKKalpha regulates IKKbeta under both basal and stimulated conditions.
AU O'Mahony A; Lin X; Geleziunas R; Greene W C
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